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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/432,503	11/02/1999	THOMAS R. CECH	15389-002611	1130

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EXAMINER

RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 01/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/432,503

Applicant(s)

CECH ET AL.

Examiner

Delia M. Ramirez

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 10/24/01.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-57 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11/2/99 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 10. 6) ☐ Other:

DETAILED ACTION

Status of the Application

Claims 41-57 are pending.

Applicant's election without traverse of Group II, original claims 2, 3, 10, 21-22, cancellation of claims 1-22, addition of claims 23-40 in Paper No. 7, filed on 9/27/01, and cancellation of claims 22-40, addition of claims 41-57 in Paper No. 9, filed on 10/24/01, is acknowledged.

Specification

1. The drawings have been reviewed and are objected under 37 CFR 1.84 or 1.152. See attached Notice of Draftsperson's Patent Drawing Review.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 41, 43, 47, 50, and 56 (claims 42, 44-46, 48-49, 51-57 dependent thereon) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 41 is indefinite in the recitation of "polynucleotide hybridizes under stringent conditions to a polynucleotide having a sequence complementary to SEQ ID NO: 1" as it is unclear absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily

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hybridize under different conditions. It is suggested that Applicants clearly indicate the degree of stringency by adding the experimental conditions required for hybridization/wash in the claim.

4. Claims 43, 47, 50, and 56 are indefinite in the recitation of "selecting cells that express an increased level of telomerase catalytic activity" because it is vague and unclear absent a reference point. The terms "increased level" are relative terms unless the activity to which the comparison is made to is defined.

5. Claims 41-57 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The method of claims 41-47 is directed to a method of increasing the proliferative capacity of mammalian cells. Although the steps of (1) introducing into the cell a recombinant polynucleotide encoding a telomerase reverse transcriptase protein and (2) selecting cells of increased level of telomerase catalytic activity are disclosed, there is no disclosure of how to determine if and/or when the proliferative capacity of a mammalian cell has increased.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 41 (claims 42-57 dependent thereon) is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

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Claim 41 is directed to a method for increasing the proliferative capacity of a mammalian cell by introducing into the cell a recombinant polynucleotide comprising the sequence that encodes a telomerase reverse transcriptase protein, variant, or fragment having telomerase catalytic activity. Applicant's disclosure points out the reasons why new methods for immortalizing cells are needed (pages 118-119 of the specification). The specification also discloses that introduction of DNA encoding a telomerase reverse transcriptase such as the telomerase reverse transcriptase of SEQ ID NO: 2 by any method known can cause any vertebrate cell to have an increased proliferative capacity or even be immortalized (page 120, lines 1-15 of the specification). Table 3 of the specification (pages 120-127) disclose a list of human cells where telomerase reverse transcriptase can be increased. However, no evidence is disclosed in the specification that transformation of cells with DNA encoding a telomerase reverse transcriptase or fragments having telomerase catalytic activity results in an increase of their proliferative capacity. No working examples are given to show that increasing the recombinant expression of telomerase reverse transcriptase in a "mortal" mammalian cell would result in an increase in proliferative capacity. A correlation of human telomerase reverse transcriptase levels and cell immortality, as disclosed in Example 2 (pages 224-225 of the specification), only shows that the mRNA levels of human telomerase reverse transcriptase in mortal cells is lower than that of immortal cell lines. None of the immortal cell lines tested were first transformed to recombinantly express human telomerase reverse transcriptase, therefore their "immortality" was not due to transformation of the cell with a recombinant nucleotide encoding a telomerase reverse transcriptase. The expression of the transcriptase measured was at steady state in all the cell lines tested (page 224, line 11 of the specification).

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The state of the art after the instant application was filed shows that expression of the human telomerase reverse transcriptase (also known as hTERT) is not sufficient for immortalization of all human somatic cells. Kiyono et al. (Nature 396 :84-88, November 1998) teaches that there is an increase in the lifespan of human fibroblasts when hTERT is expressed but hTERT expression alone is not sufficient for the immortalization of other cells such as human keratinocyte or mammary epithelial cells (Abstract). Their results indicated that inactivation of the Rb/p16 pathway is required in addition to telomerase activity to achieve immortalization of human keratinocytes and mammary epithelial cells (page 87, second column, lines 3-6). Kiyono et al. also disclose that immortalization by expression of hTERT alone was probably cell-specific because of the differences in the regulation of senescence in different cells (page 87, second column, lines 10-13). O'Hare et al. (PNAS 98 :646-651, January 16, 2001) discloses that there are several conflicting reports on the effect of hTERT expression alone as a way to achieve immortalization of human somatic cells (page 646-651, second column, lines 10-22). O'Hare et al. shows that expression of hTERT alone is not enough to achieve immortalization of human mammary fibroblasts and endothelial cells. Only after a temperature-sensitive mutant of simian virus 40 large-tumor antigen was co-expressed with hTERT, did the human mammary fibroblasts and endothelial cells become immortal (page 646, column 1, Abstract, lines 4-12; page 650, second column, lines 22-26; page 651-12, first column, lines 1-9).

Therefore, due to the lack of relevant examples, the amount of information provided, the unpredictability of the prior and current state of the art in regard to telomerase reverse transcriptase activity and cell proliferation, one of ordinary skill in the art would have to go through the burden of undue experimentation to determine if the claimed method can be used as

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disclosed in any mammalian cell. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to use the invention in the manner reasonably correlated with the disclosed usage.

7. No claim is in condition for allowance.

Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. **NO DUPLICATE COPIES SHOULD BE SUBMITTED**, so as to avoid the processing of duplicate papers in the Office.

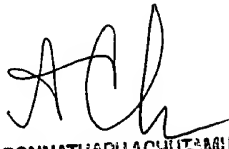
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
January 14, 2002


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